

Report of the NIGMS Glue Grant Program Interim Outcomes Assessment Meeting

Chairperson's Report by Dr. Norma M. Allewell

Summary:

A panel of sixteen scientists met on March 21-22, 2011 to conduct an outcomes assessment of the NIGMS Large-Scale Collaborative Project Awards (Glue Grant) Program and to advise NIGMS about whether to continue the program and how to structure this and/or related grant programs in the future. Members of the NIGMS Glue Grant Assessment Organizing Committee attended both closed and open sessions. NIGMS program officers, scientific liaisons, and both NIGMS management and members of the public were present during open sessions. The panel reviewed five Glue Grant projects that had been funded for five or more years and considered bibliometric data, web accession data, and input from the broader scientific community obtained through online surveys. The panel agreed that the goals, organization, and degree of success of the individual projects were highly variable. Two projects were viewed by the majority of the panel as having achieved substantial success, while at least one was viewed as having significant flaws. A strong majority of the panel (13 in favor, 2 opposed, 1 abstention) voted that the program as currently constituted should not be continued. However, the panel voted unanimously that NIGMS should continue to fund new award programs outside the RO1 mechanism to support innovative, interdisciplinary, large scale research. Most felt that a suite of programs with smaller but more numerous awards was probably needed to replace different aspects of the Glue Grant Awards Program.

Report:

The Principal Investigators and NIH staff of the Glue Grant Awards that were reviewed by the panel reported the following major accomplishments:

The Alliance for Cell Signaling identified new elements of the signaling circuits that regulate cellular responses to physiological and pharmacological stimuli by G-coupled protein receptors in murine B cells and macrophages. The Alliance also characterized changes in cAMP production, Ca^{+2} increases, and cytokine release. Several technological developments and reagent collections were shared with the community and have been transferred to vendors. Databases that were developed have been made available through the *Nature* Signaling Gateway.

The Cell Migration Consortium identified new migration-related molecules; determined posttranslational modifications and interactions of the migratory proteome; defined the structures of large, migration-related supramolecular assemblies; developed probes and technology to locate, quantify, perturb spatially and temporally regulated signals; produced conditional knock-out and knock-in mice and cell lines for key migration related genes; developed mathematical models of migration that stimulated production of quantitative data; and developed technologies for studying migration in tissues.

The Consortium for Functional Glycomics developed a set of novel resources for the glycan binding protein community, including a library of synthetic carbohydrates; glycan and glycogene microarrays; knockout mouse strains deficient in key genes and enzymes; core facilities for analyzing glycans and phenotyping novel transgenic mice; specialty databases; and novel interfaces. Examples of biomedical issues investigated by the consortium include the role of receptor specificity in influenza virulence, the role of C-type lectins in innate immunity, the roles of galectins in modulating innate and adaptive immune responses, and the role of siglecs in innate immunity.

The Lipid Metabolites and Pathways Strategy project provided a detailed analysis of the lipidome of the mouse macrophage, changes in the lipidome resulting from various stimuli, and the genes and proteins involved in these changes. The project synthesized 500 mass spectrometry lipid standards, developed bioinformatic and systems tools, and provided new insights into the interaction of lipid pathways under normal and disease conditions.

The Inflammation and Host Response to Injury project developed a consensus with regard to standardized patient treatment and data protocols; new microarray chips; a new paradigm for host response to injury; microfluidics approaches for blood collection and data processing appropriate for community hospitals; and compiled and disseminated large clinical data sets, with appropriate IRB approval. Trauma patients treated using the standardized protocols developed by this project appear to have reduced morbidity and mortality.

Assessments of each of these programs by panel members who are experts in the area were followed by extensive discussion by the entire panel. Accession data from the *Nature* Gateway websites for individual programs, preliminary results from an ongoing bibliometric analysis, and the results of an online community survey with a very small (127) number of respondents were also considered. There was broad agreement that the goals, organizational structure, and degree of success of the five projects were highly variable. Two projects were judged by the majority of the panel to have made substantial contributions to their fields. While concerns were identified, one of these projects was characterized as “having enormous impact” and “propelling the field forward in ways that couldn’t otherwise be achieved”. Two were regarded by the majority of the panel as having mixed success, while one was regarded as having significant flaws. The most successful projects had well defined goals, teams with the range of expertise (often multidisciplinary) required to meet those goals, leaders who were attuned to the needs of the community, the capacity to take risks and evolve with time, effective outreach to the community, robust informatics components, and effective oversight by NIGMS staff. Conversely, projects deemed less successful tended to have one or more of the following issues: goals that were not right-sized (either too sweeping or too narrow) and/or inflexible, ineffective community engagement and outreach, missing expertise (often informatics), and inadequate oversight and accountability. With only two exceptions, dissemination of information and data was seriously compromised by the quality of the databases, web interfaces, and analytical and querying capabilities of the informatics resources that were developed.

In identifying the successes of the Glue Grant Awards Program as a whole, the panel concluded that all five projects had made scientific contributions that range from significant to major, and two were viewed as having made substantial contributions to their fields. In several projects, funding provided by the Glue Grant Program supported development of unique methods, technologies, and research tools that might not otherwise have occurred. The majority of the programs increased the level of collaboration and multidisciplinary research, enabled increases in research personnel, infrastructure, and probably stimulated funding from other sources. Importantly, the Glue Grant Awards Program provided a model for the development of large-scale, hypothesis driven, cross-disciplinary integrative biomedical science, at a time when the need for such programs was receiving attention. In addition, the successes and challenges of the Glue Grant Awards Program provide a useful guide for the development of future programs.

After extensive discussion, a strong majority of the panelists concluded that, despite the successes of some of the projects, the scope and impact of the scientific knowledge outcomes of the Glue Grant Awards Program as a whole were not commensurate with the investment. While a minority felt that the scale of the GLUE program was justified by the critical importance of large, cross-disciplinary initiatives of this type to the future of science, the majority strongly questioned whether grants of this size are justified at a time when many investigators, particularly young investigators, are experiencing severe difficulty in obtaining and sustaining funding. The absence of ongoing peer review to inform decisions about funding individual projects was a major concern. Some panelists felt that the same results could have been achieved in more than one program with RO1 and/or Program Project grants and with substantially less funding. In some cases, the question of whether the whole was actually less than the sum of the parts was raised. There was widespread dissatisfaction with the extent to which information and data were disseminated to the community, and, in some cases, dissatisfaction with the extent to which the community was consulted and engaged. **As a result, a large majority of the panel (13 in favor, 2 opposed, 1 abstention) voted that the Glue Grant Awards Program as constituted should not be continued.** Subsequently, the panel unanimously endorsed the creation of a suite of modified program(s) to support innovative, interdisciplinary, large scale research. Most panelists agreed that awards should be considerably smaller, but larger in number.

The panel discussed at length the criteria that must be met in order to create successful successors to the Glue Grant Award Program and identified the following:

- A relentless focus on important problems, as defined by the scientific community, that are high risk/high gain, offer economies of scale, require a multi-disciplinary approach, and are ripe for development.
- A rigorous review process, with the expertise of panelists encompassing all dimensions of the proposed projects, and with very high standards.
- Well defined deliverables that will be of value to the community at large.
- A highly capable management team, with a leader attuned to the needs of the community and with a track record of inclusivity.

- Research teams that encompass all the types of expertise required, from biology to bioinformatics.
- Close oversight, at a variety of levels, from inception to completion, with the recognition that substantial mid-course corrections are likely to be required as fields evolve and discoveries are made, and that marginally successful programs may need to be terminated.
- A robust informatics component, staffed by experienced professionals, which meets current data representation standards and has sophisticated analytical, querying, and visualization software tools.
- A well-developed plan for ensuring that databases, new technologies, core research facilities and other products of the grant are sustained after the grant expires.

The panel made a number of suggestions about the administration of such programs. Most panel members felt strongly that the average size of an award should be greatly reduced relative to the Glue Grant Award Program, and that there should be a greater range in the size and length of awards. Some felt that the current requirement, that all investigators hold an RO1 grant should be relaxed, in part to enable more participation by engineers, computer scientists and physical scientists. To increase participation and the quality of proposals, panel members suggested more vigorous advertising of the program, and more frequent calls for proposals. Several panel members suggested that an explicit plan for training the next generation should be a requirement of the program. To ensure that the knowledge and data acquired are readily accessible for use by the scientific community during and after the completion of the program and that the costs are sustainable, the suggestion was made that, where appropriate, the National Center for Biotechnology Information (NCBI) of the National Library of Medicine be the repository for databases developed through this and subsequent programs, and that the NCBI be involved at all stages of the program, including development of the RFA. The panel also advocated vigorous efforts to commercialize new technologies when appropriate to ensure that their full potential is realized and that they are widely available.